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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,911	04/17/2001	Gyula Hadlaczky	24601-402I	7763

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EXAMINER

SHUKLA, RAM R

ART UNIT	PAPER NUMBER
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1632

19

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/836,911

Applicant(s)

HADLACZKY ET AL.

Examiner

Ram R. Shukla

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) None is/are allowed.
- 6) ☒ Claim(s) 23-60 is/are rejected.
- 7) ☐ Claim(s) None is/are objected to.
- 8) ☐ Claim(s) None are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Response filed 6-23-03 has been received and entered.
2. Claims 23-60 are pending in the instant application.
3. As noted in the previous office action, the effective filing date for the claimed invention is assigned 4-10-1997, the filing date for application 08/835682, to which instant application (09/836,911) claims priority as a continuation.
4. Formal drawings have been received.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 23-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office action of 12-18-2002.

Response to Arguments

Applicant's arguments filed 6-23-03 have been fully considered but they are not persuasive. Applicants first argue that reliance on post-filing date references to establish a lack of enablement is improper. This argument is not persuasive since several publications that covered the state of the art from the date of filing of the application to the present were used to demonstrate that the state of the art of making a transgenic animal by using the method of the claimed invention was not predictable and therefore the claimed invention was not enabled. On page 4 of the

response, applicants cite several case laws, however, these case laws are not relevant because the issue at hand is not the enablement of every species, rather the issue is of the enablement of the full scope of the claimed invention.

Applicants' attention is drawn to other case laws, which deal with inventions where the state of the art is unpredictable (MPEP 2164.03). For example,

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling."

"However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work."

It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991).

Page 7 of the applicants' response reiterates the description of the invention while page 8 states that the level of skill is high and again on pages 8-10, the teachings of the specification are reiterated. Applicants argue that Wilmut 1997 Nature article provides enabling disclosure and that there is no requirement under

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current law specifying that the method must be fully reproducible every time it is practiced. In response it is noted that a specification should provide an enabling disclosure to enable the full scope of the claims. In the instant case, the specification incorporates a process that has been found to be non-reproducible in the art. Since the specification does not disclose a working example, an artisan would not know whether the method will work in the light of the art of record that indicates that the method was not reproducible or in other words could not be practiced with the given disclosure. Applicants argue that the articles of Wolf et al and Sgamarella et al do not provide any evidence that it would involve undue experimentation. However, these arguments are not persuasive because the specification does not teach how would an artisan have corrected the problems of the method of Wilmut et al. Further applicants have cited the article by Schnieke et al in the support of their arguments that Wilmut et al method is reproducible. However, Schnieke et al did not exactly follow the method of Wilmut et al, for example, the source of the nuclei were different, the culture methods were different etc. And these improvisations are not taught in the specification.

Next, applicants have discussed the knowledge of those of skill in the art (pages 15-18) and argue that procedures relating to DNA manipulations etc. were well known in the art, however, these arguments are not persuasive because the issue is not of basic skills but it is of making transgenic animals by nuclear transfer and by introducing gene of interest in a cell using artificial chromosomes and this is what was not routine in the art at the time of invention. Contrary to applicant's arguments, the specification did not teach any specific teachings as to how to practice the claimed invention except for general description of the methods. As discussed in the previous office action, the specification does not provide any specific teachings for correcting the limitations faced by an skilled artisan, such as the state and development and cell cycle of donor cells, the choice of the recipient cell, the methods of activation of the oocytes, cell cycle coordination between donor cell and the recipient cytoplasm and the method for fusion between nuclear donor and recipient cytoplasm etc. It is reiterated that the specification does not provide

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any specific teachings to practice the claimed invention of making transgenic animals as recited.

Case laws states:

"It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." (See *Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966))

Applicants, on page 19, argue that they have disclosed working examples by citing parts of the specification, however, none of these working examples teach how to make a transgenic animal as recited in the claimed invention. Next, in pages 20-23 discuss predictability and discuss different references used in the enablement rejection and argue that post filing arts cannot be used in enablement rejections. However, applicants have ignored the fact that the papers used were published in 1999, 2000 and 2002 which cover the entire period from the date of filing to present and therefore present the state of the art of making transgenic animals and artificial chromosomes from the date of filing to the present. Next applicants argue that selective reading of the references have taken statements out of context regarding the limitations of nuclear transfer and that the examiner has equated "limitations" with "unpredictability". Applicants' arguments are not persuasive because limitations have not been equated with unpredictability, rather limitations have been discussed because that's what will be faced by an artisan when practicing the claimed invention and when the specification of record at time of filing lacks teachings to address these limitations, an artisan has to address these limitations.

It is noted that these limitations are not routine and therefore the experimentation to address these limitations will not be routine. It is emphasized that it is these limitations why the methods of Wilmut et al discussed above are not enabling. Furthermore, the enablement rejection discussed specific scientific issues and applicants did not address as to how the specification addressed these scientific issues. As noted in the previous office action, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

In conclusion, the specification as filed is not enabling for the claimed invention because the state of the art of producing transgenic animals from any donor cell into any recipient cell and for transfer of artificial chromosomes in a cell that could serve as donor cell was not predictable and an artisan of skill would have required extensive experimentation to practice the claimed invention and such experimentation would have been undue since the experimentation was not routine, and the state of the art was unpredictable and the specification did not teach how to address the limitations and unpredictable nature of the invention.

7. No claim is allowed.


THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

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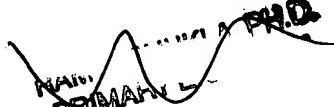
calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.



RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

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